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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/967,321	10/01/2001	Jonathon Michael Blackburn	0623.0860002/LBB/Y-W	4288

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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
04/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/967,321	BLACKBURN ET AL.	
	Examiner	Art Unit	
	ANN Y. LAM	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,13,18-24,26 and 27* is/are pending in the application.

4a) Of the above claim(s) *8-12,14 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,13,18-24,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-4, 13, 18-24, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morin et al., 6,610,839, in view of Chin et al., 6,197,599.

Morin et al. discloses the invention substantially as claimed. As to claim 1, Morin discloses a method comprising

(a) inserting a marker DNA sequence in frame immediately preceding a stop codon of each of a plurality of target DNA sequences to form a plurality of modified DNA sequences which encode a plurality of modified amino acid sequence each comprising a marker moiety (col. 156, lines 20-25) (it is understood that a plurality of modified DNA sequences are encoded, see for example col. 155, lines 29-30, disclosing producing of large quantities of hTRT using *Picha pastoris* expression vector pPICZ B, and col. 156, lines 16-18, disclosing a second *Picha pastoris* expression vector derived from pPICZ B);

(b) expressing the plurality of modified amino acid sequences from the plurality of modified DNA sequences (col. 156, lines 25-29);

(c) purifying and immobilizing each of the plurality of modified amino acid sequences into contact with a solid support wherein the marker moiety of the plurality of modified amino acid sequences is directly attached to the solid support (col. 43, lines 27-34), disclosing the isolation of the proteins by binding the $(HIS)_6$ to resins containing nickel ions, i.e., metal-chelate affinity chromatography, which is a direct attachment to the solid support, as is also disclosed by Applicants' specification) (the isolation step disclosed by Morin et al. is both the step of immobilizing and purifying in a single step, as is also disclosed by Applicants' specification), and

(d) washing said solid support to remove unbound proteins (col. 43, lines 30-34).

Moreover, while Morin et al. teaches use of the fusion protein system to isolate specific proteins and peptides (col. 43, lines 27-29), Morin et al. however does not teach that the bound proteins are in an array. This limitation is taught by Chin et al.

Chin et al. teaches that proteins immobilized on a solid support can be immobilized in an array, or specific position, so it can be identified by its position and further characterized thereby allowing for study of a wide variety of proteins in a single experiment by a large number of proteins on a support (col. 2, line 60 – col. 3, line 3.) It would have been obvious to one of ordinary skill in the art at the time the invention was made to form the immobilized proteins in the Morin et

al. invention in the form of an array as taught by Chin et al. for the advantage of identifying a protein based on its position and studying a wide variety of proteins in a single experiment for convenience.

As to the following claims, Morin et al. discloses the limitations as follows.

As to claim 2, the tag is a peptide sequence (col. 156, line 22).

As to claim 3, the tag allows for purification of the individual proteins in the array (col. 43, lines 27-29).

As to claim 4, the tag is inserted such that the start or stop codon for each of the proteins is replaced (column 156, lines 22-23).

As to claims 13 and 26, the array is used to immobilize specific antibodies (col. 43, lines 34-35).

As to claim 18, the protein array comprises kinases (col. 26, line 26.)

As to claim 19, the plurality of modified amino acid sequences are modified human amino acid sequences (see abstract, "human telomerase reverse transcriptase").

As to claim 20, Morin et al. teaches a FLAG marker moiety (col. 153, line 54.)

As to claims 21-23, the marker moiety is post-translationally modified (col. 49, line 44), such as addition of a lipid (col. 49, line 43), and the modified amino acid sequences are folded into the correct formation (col. 49, line 45.)

As to claim 27, Morin et al. teach using nickel ionon for metal-chelate affinity chromatography to bind polyhistidine tracts $(HIS)_6$.

2. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Morin et al., 6,610,839, in view of Chin et al, 6,197,599, and further in view of Ben-Bassat et al., 4,865,974.

Morin et al. in view of Chin et al. disclose the invention substantially as claimed (see above with respect to claim 1), except for the steps of digesting the target DNA sequence, annealing the marker DNA sequence and ligating the marker DNA sequence as claimed by Applicant. Although Morin et al. teaches that the hTRT stop codon is removed and replaced by vector sequences encoding for the Mye epitope and the His6 reporter tag (col. 156, lines 22-25), Morin et al. does not specifically disclose the steps for removing and replacing the DNA sequences. Ben-Bassat et al. teaches that the steps of digesting, annealing and ligating are well known in the art for removing and replacing DNA sequences.

Ben-Bassat et al. teaches that construction of suitable vectors containing the desired coding and control sequences employs standard ligation and restriction techniques which are well understood in the art (col 8, lines 3-6.) Bassat et al. teaches restriction enzymes for digestion of DNA sequences (col. 8, lines 9-10), annealing (col. 8, line 53) and ligation steps (col. 8, line 59.) It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the steps of digestions, annealing and ligation as taught by Ben-Bassat et al. for the steps of removing and replacing DNA sequences in the

Morin et al. method because Ben-Bassat et al. teaches that these steps are well known in the art for removing and replacing DNA sequences.

3. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Morin et al., 6,610,839, in view of Chin et al, 6,197,599, and further in view of Orr et al., 5,741,645, and Nielsen et al., 6,350,853.

Morin et al. in view of Chin et al. disclose the invention substantially as claimed (see above), except for two markers, one immediately following a start codon and one immediately preceding a stop codon. Orr et al. discloses this limitation.

Orr et al. teaches the use of two flanking markers for the advantage of isolating region-specific DNA markers (col. 16, lines 40-44.) Moreover, Nielsen et al. teaches a marker sequence immediately following a start codon (col. 33, lines 23-26.) It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide two flanking markers as taught by Orr et al. in the Morin et al. method because Orr et al. teaches that it provides the advantage of isolating region-specific DNA markers, and it would have been obvious to one of ordinary skill in the art to provide the second marker immediately following a start codon as taught by Nielsen et al. as a known location for inserting a marker. Also, Applicant has not disclosed a use for inserting a marker immediate to the start codon that is a different use from that shown in the prior art.

Response to Arguments

Applicants' arguments filed December 17, 2007 has been considered but is not persuasive.

Applicant states that Morin does not teach or suggest that the single target sequence can be modified in a single reaction. Examiner however that the claims do not require such limitations. Applicant also states that the manipulation of this sequence in two vectors does not constitute "a plurality of target sequences", which is understood in the art to mean "a library of cDNA molecules" Examiner disagrees as the same terminology can also be used in the art to simply mean a plurality of target sequences. Given its broadest reasonable interpretation, the term does not require that the target sequences be different in any way.

Applicant further argues that the purification and immobilization as described by Morin does not relate to a single support but to many similar supports within the resin, And that Morin does not teach or suggest the purification and immobilization of tagged proteins in a single step, as well as their immobilization in a spatially-define format. As to the argument regarding the limitations "in a single step", because Morin discloses the same method. As to the argument regarding 'spatially defined", Morin is not relied upon by Examiner to teach such limitation, but rather the Chin reference is relied upon for such teaching and motivation or other reason to modify the Morin invention accordingly. For the same reason, the arguments regarding the deficiencies of Chin in failing to beads a method for purifying and immobilizing a plurality of

tagged amino acid sequences directly to a solid support via a marker tag moiety in a single step are not persuasive, as Examiner relies upon Morin for such step limitation.

Applicant also argues that Orr is silent as to inserting a marker DNA sequence immediately following a start codon or immediately preceding a stop codon as claimed by Applicant. Applicant states that these naturally occurring dinucleotide repeats disclosed b Orr are present in chromosome and are not inserted. Examiner does not find this persuasive as the usefulness of markers at the claimed locations are taught in the art, even if in separate references and provided in different ways. The modifications obtained by combining the prior art teachings yield a predictable outcome for the same purposes or benefits as disclosed in the prior art references, which thus renders such modifications predictable.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory

action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Riggs et al., 6,593,120, disclose a method inserting histidine tag immediately preceding a stop codon, or before a start codon and expressing the protein, and isolating the protein through immobilizing the histidine tag on a column with nickel ions (col. 24, lines 23-24, col. 25, lines 13-19, col. 26, lines 37-47, col. 27, lines 33-36, and col. 5, lines 36-39).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on M-Sat 11-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ann Y. Lam/

Primary Examiner, Art Unit 1641